

Application No. 10/559,694  
Reply to Office Action of February 5, 2010

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Docket No.: 64609(70301)

**REMARKS**

In the Office Action dated February 5, 2010, claims 1-9 and 11-19 are pending in this application, claims 3, 5-7, 13-16 and 18 are withdrawn from consideration, and claims 1, 2, 4, 8, 9, 11, 12, 17 and 19 are rejected. Reconsideration is requested for at least the reasons discussed hereinbelow. The rejection is made final.

Applicant requests that the finality of this rejection be withdrawn in view of the newly applied references - Grofte and Garcia-Tsao (as stated at page 5, line 1 of the Office Action). Applicant has not had a chance to consider and respond to the rejections based on the use of these references. Thus, positions regarding these new references have not been developed for the record.

Claims 1, 8, 9, 11, 12, 17 and 19 are rejected under 35 U.S.C. §103(a) over Fryburg et al (WO 02/0604220A2; "Fryburg") in view of Grofte et al (US 2002/0028764 A1; "Grofte").

The invention, as set forth in claim 1, is directed to a method for the therapy of a human diagnosed with portal hypertension, the method comprising administering an anti-portal hypertension effective dose of an inhibitor of phosphodiesterase type 5 (PDE 5), or of a pharmaceutical composition containing a PDE 5-inhibitor, wherein the PDE 5-inhibitor is administered to said human.

Fryburg discloses the use of vardenafil for the treatment of diabetes type 2. As admitted by the Examiner, Fryburg fails to teach or suggest administration of vardenafil to a human diagnosed with portal hypertension or the dosage for such administration.

Grofte discloses the administration of IGF-1 to chronic liver disease patients who frequently suffer from low IGF-1 levels. Chronic liver disease is frequently accompanied by a lack of IGF-1 (see also, Moller et al., Hypertology 1996; 23(5): 10731078). It is noted that IGF-1 as used in Grofte may alleviate the defects in glucose metabolism in a patient but does not have any effect whatsoever on portal hypertension. In fact, document US 2002/0028764 A1 – beyond the fact that it has no relation whatsoever with PDES- inhibitors such as vardenafil - mentions portal hypertension

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(see [0179], [0223]) without any reference to a common pathogenic mechanism linking portal hypertension and diabetes type 2. The document does therefore not provide any suggestion for a skilled person that curing diabetes may also alleviate portal hypertension itself.

The Examiner asserts that, because Grofte discloses that diabetes type 2 and portal hypertension *may* occur in combination, it would have been obvious to one of ordinary skill in the art to administer the treatment of Fryburg for the therapy of a patient diagnosed with portal hypertension.

Applicant strongly disagrees. There is absolutely no suggestion in the combination of Fryburg and Grofte that vardenafil would be useful for the treatment of portal hypertension. The fact that portal hypertension may occur in combination with diabetes type 2 provides no suggestion that a treatment for diabetes type 2 can be used to treat portal hypertension. Fryburg relates to the use of vardenafil for the "curative palliative or prophylactic treatment of type 2 diabetes mellitus" (see abstract). No suggestion is to be found anywhere in Fryburg that vardenafil may also have an impact on portal hypertension. Grofte fails to make up for the deficiencies of Fryburg. Grofte also has no suggestion anywhere that vardenafil may also have an impact on portal hypertension.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of any combination of Fryburg and Grofte.

Claims 2, 4, 8, 9, 11, 12 and 19 are rejected under 35 U.S.C. §103(a) over Fryburg in view of Grofte and further in view of Garcia-Tsao.

The invention, as set forth in claim 2, is directed to a method for the therapy of a human diagnosed with one or more of the following diseases or complications in humans, bleeding complications of the portal hypertension, hepato-renal syndrome, hepato-pulmonary syndrome, hepatic encephalopathy, spontaneous bacterial peritonitis and ascites, the method comprising administering to said human a portal blood flow increasing amount of an inhibitor of

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phosphodiesterase type 5 (PDE 5), or of a pharmaceutical composition containing a PDE 5-inhibitor.

Fryburg and Grofte are discussed above. Further, as admitted by the Examiner, Fryburg and Grofte fail to teach or suggest the administration of vardenafil to a patient diagnosed with bleeding complications of portal hypertension, including bleeding from the esophagus and/or fundus varices.

Garcia-Tsao fail to make up for the deficiencies of Fryburg and Grofte. Garcia-Tsao fail to teach or suggest that vardenafil would be useful for treating portal hypertension, much less for treating bleeding complications of portal hypertension, including bleeding from the esophagus and/or fundus varices.

The fact that bleeding from esophageal varices is a common complication of portal hypertension is not a substitute for a suggestion that such bleeding can be treated by use of vardenafil.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of any combination of Fryburg, Grofte and Garcia-Tsao.

The Examiner contends that the inventions set forth in the currently pending claims would have been obvious because "the instant claims are not limited to the treatment of portal hypertension or its complications, only the therapy of a human diagnosed with the conditions." This statement is not understood. None of the cited prior art, whether taken alone or in combination, suggest that it would be useful to treat a human diagnosed with portal hypertension with vardenafil or any PDE 5 inhibitor. Thus, it is not seen how it would have been obvious to one of ordinary skill in the art to use vardenafil or a PDE 5 inhibitor to treat a human diagnosed with portal hypertension. On the other hand, based on the teachings of Fryburg, it would have been obvious to treat a human diagnosed with diabetes type 2 with vardenafil. However, it is not seen how that would have made the currently claimed invention obvious to one of ordinary skill in the art.

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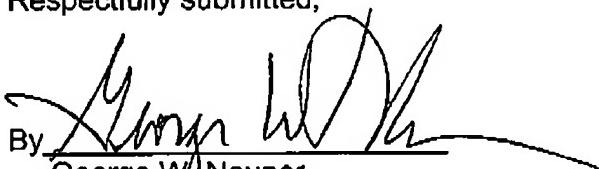
If for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, the Commissioner is hereby authorized and requested to charge Deposit Account No. 04-1105.

In view of the discussion above, Applicant respectfully submits that the pending application is in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

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Respectfully submitted,

By

  
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